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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

DETAILED ACTION

Request for Continued Examination

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/10/2008 has been entered. Claims 1, 3-4 and 38 are currently under examination.

Response to Arguments

Applicants argue over the 35 USC 112 first paragraph rejection concerning new matter that it is clear to one skilled in the art that the present invention does not involve Alzheimer's disease but a different condition resulting from low LDL. Applicants feel that they should be able to claim the invention in such broad terms.

The above arguments are not persuasive as detailed in the Advisory Action mailed on 3/19/2008. As discussed previously, there is no teaching in the specification that the treatment is not intended for those who are being treated for Alzheimer's disease. Accordingly, the rejection is maintained.

Applicants argue over the 35 USC 112 first paragraph rejection that because they have amended claim 1 to limit the active compounds to nicotinic allosteric potentiators, this is a sufficient amendment to overcome the rejection.

This argument is not found persuasive because as was discussed in the Advisory Action, there is no teaching that all nicotinic allosteric potentiators will effectively treat all cognitive dysfunctions. The Examiner has previously pointed out that the present application supports the use of galanthamine but not all nicotinic allosteric potentiators.

Because claims 37 and 39 have been cancelled, any rejection to those claims is withdrawn. However, these claims were not rejected alone and any rejections involving those claims may still be applied if it is applicable to any pending claims.

It should be noted that claim 1 presently reads is on a method for treating a cognitive dysfunction of a patient associated with low LDL-cholesterol values in serum by modulation of nicotinc receptors and is how the claim is being treated for prior art purposes.

Regarding the 35 USC 103 rejection, the Applicants assert that the claims exclude patients who are being treated for Alzheimer's. Applicants assert that prior to the present invention, there was nothing in the art to point one towards administering galanthamine to those having low LDL cholesterol values. Applicants argue that Kivipelto is not teaching the administration of statins in the presence of dementia but treating hypercholesterolemia in midlife to nondemented people. Applicants also point to Table 3 and conclude that there was a higher incidence of AD in those receiving cholesterol lowering agents.

As discussed previously, it was not suggested by the Examiner that there is motivation to administer an Alzheimer's drug to patients with high cholesterol values. Kivipelto was used to teach that high serum cholesterol increases the risk of

Alzheimer's disease. This is the purpose of the article written by Kivipelto and Kivipelto concludes the article by stating that the study showed that raised systolic blood pressure and high serum cholesesterol concentrations in midlife increased the risk of Alzheimer's disease in later life (see discussion).

Further, Applicants give a detailed description of several papers to argue that the present invention was not known at the time the invention was filed. In response to this, it is noted that there are flaws presented in all of the articles that were presented. For example, Rockwood admits to issues associated with the study, but concludes that the results from their study indicate a lower risk of dementia after treatment of lipid-lowering agents and agree that further research is warranted. Therefore, while it is acknowledged that questions arise from the studies performed at the time, there is a general consensus that more studies are needed which is often the consensus in clinical reports especially in an undeveloped area of study. Therefore, there is no definitive conclusion from the papers presented that there is no correlation.

Accordingly, the rejections are maintained and given below for Applicant's convenience.

Claim Rejections – 35 U.S.C. § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-4, and 37-40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Amendment to the claims in which it is stated "...other than one being treated for Alzheimer's disease with a nicotinic allosteric potentiator...." is not supported in the specification and is considered new matter.

Claims 1, 3-4 and 38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of the cognitive dysfunction Alzheimer's disease of a patient associated with low LDL-cholesterol values (claims 1, 3-4 and 38) with galanthamine, does not reasonably provide enablement for treating all cognitive dysfunctions associated with low LDL-cholesterol values with all nicotinic allosteric potentiators. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547

the court recited eight factors: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) The nature of the invention and breadth of the claims: The rejected claims 1, 3-4 and 38 are drawn to a method for treating cognitive dysfunction (claims 1, 3-4, 38) of a patient associated with low LDL-cholesterol values in serum by modulating nicotinic receptors comprising administration of a nicotinic allosteric potentiator. The claims are considered very broad because the claims are directed to method for treating any cognitive dysfunction caused by low LDL-cholesterol values in the brain, without specifying which dysfunction is being treated and to treatment with any nicotinic allosteric potentiator.

(2) The state of the prior art: The state of the art regarding treating cognitive dysfunction caused by low LDL-cholesterol in the brain by modulating nicotinic receptors by administration of nicotinic allosteric potentiators is not well described, for example see Messer (Curr Topics Med Chem, 2002, 2, 353-358). Messer teaches that the clinical utility of cholinergic agonists in the treatment of AD has been limited due to side effects or lack of efficacy (see Summary). Further, there is no description in the art that all nicotinic allosteric potentiators will treat cognitive or neuromuscular dysfunctions.

(3) The relative skill of those in the art: The relative skill of those in the art is high.

(4) The amount of guidance or direction presented and the presence or absence of working examples: In the instant case, the specification discusses the use of nicotinic modulators to be used in the present invention without actual instruction. Applicants discuss the usage of galanthamine in Alzheimer's disease, which is art recognized. However, Applicant's give a limited discussion of compounds suitable for the invention and give no working examples proving their actual effects on all cognitive dysfunctions. The specification provides no working examples of treating all cognitive impairments caused by low brain LDL by modulating nicotinic receptors by administration of nicotinic allosteric potentiators. Note that lack of a working example is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art. See MPEP § 2164.

(5) The quantitation of experimentation necessary: As stated above, the rejected claims 1, 3-4 and 38 are drawn to a method for treating cognitive dysfunction of a patient associated with low LDL-cholesterol values in serum by administration of an effective amount of a nicotinic allosteric potentiator. The specification provides no working examples that all nicotinic allosteric potentiators will effectively treat all cognitive dysfunctions. Applicant fails to provide information sufficient to practice the claimed invention, absent undue experimentation. Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling

disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Claim Rejections - 35 U.S.C. § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3-4 and 38 rejected under 35 U.S.C. 103(a) as being unpatentable over Davis et al. (U.S. Patent #4,663,318) in view of Kivipelto (BMJ (2001) 322: 1447-1451) and Simons et al. (Neurology (2001) 57: 1089-1093).

Davis et al. teach that galanthamine is useful for the treatment of Alzheimer's disease (see whole document).

Davis et al. do not specifically teach that the patient population receiving the treatment is associated with low LDL-cholesterol values or that the low cholesterol values are a result of treatment with HMG-CoA reductase inhibitors.

Kivipelto et al. teaches that high serum cholesterol increases the risk of Alzheimer's disease (pg. 1449, first paragraph and Table 2).

Simons et al. teach that there is a decreased prevalence of Alzheimer's disease associated with the use of statins (pg. 1091, paragraph 2). It is taught that statins cross the blood-brain barrier and decrease de novo cholesterol synthesis by inhibiting HMG-CoA reductase (pg. 1091, paragraph 2).

It would be obvious to one having ordinary skill in the art at the time of the invention to add to the drug regimen of an elderly patient that suffers from a cognitive disorder and is taking statins for hypercholesteremia, an effective amount of galanthamine to improve cognitive behavior because Davis teaches that galanthamine is effective in treating Alzheimer's disease, which is a disease of cognitive impairment. One would have been motivated to do so because the prior art teaches that high levels of cholesterol and Alzheimer's disease are related (as taught by Kivipelto), and that patients receiving statins for hypercholesteremia have a lower incidence of Alzheimer's disease (as taught by Simons); therefore, one would have a reasonable expectation of success with treatment of galanthamine for a cognitive disorder.

Furthermore, Applicant has not provided any evidence showing the criticality of cholesterol levels at 109 mg/dl. Accordingly, identifying suitable patients by observing their cholesterol levels during hypercholesteremia treatment would be achieved by routine experimentation.

Conclusion

No claims are allowed.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Renee Claytor whose telephone number is (571)272-8394. The examiner can normally be reached on M-F 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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